II. REMARKS

These remarks are in response to the Office Action mailed July 3, 2001. Applicants submit that the amendments to the claims are for clarity and should not be construed as amendments affecting patentability under *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). Additionally, new claims 28 and 29 have been added. As drafted, these claims are fully supported by the specification, as filed, and do not add new matter. Thus, upon entry of the amendment, claims 17-29 are under examination.

A. OBJECTION TO THE SPECIFICATION

The specification of the present application was objected to due to the following informalities, as set forth in Paper No. 12: the ATCC number, for example, on pages 3 and 6, is not specified, there is no description of Figures 9 and 10, the description of Figure 11 is incorrect, the specification incorporates expired provisional application 60/008,316 by reference, the specification does not contain sequence identifiers in all instances where the specification discusses sequences, and the paper copy and electronic copies of the Sequence Listing are different. As these objections have been remedied by the amendments of the present Response, it is respectfully requested that the above objections be withdrawn.

It is respectfully submitted that the reference to the ATCC number on pages 3 and 6 has been removed, as set forth above. As the language is no longer present in the specification, it is respectfully submitted that the objection is moot.

As the amendments set forth above provide accurate descriptions of Figures 9, 10 and 11, it is respectfully requested that the objection to these figures be withdrawn.

The specification is objected to in that expired provisional application 60/008,316 is incorporated by reference. It is respectfully submitted that an application was filed, claiming priority to provisional application 60/008,316 prior to expiration of the provisional application.

The amendment to the specification above has incorporated the serial number of the new U.S. Patent Number claiming priority to Provisional Application Serial Number 60/008,316. It is therefore respectfully submitted that this amendment remedies the incorporation of an expired application. As such, it is respectfully requested that the objection be withdrawn

The specification is also objected to, in that sequence identifiers are not used in all instances. It is respectfully submitted that the amendments to the specification, particularly those amendments made to the last two paragraphs on page 27, remedy the lack of sequence identifiers. It is therefore respectfully requested that the objection be withdrawn.

The application is also objected to in that the application fails to comply with the requirements for applications having nucleotide and/or amino acid sequences under 37 C.F.R. §§1.821-1.825. It is respectfully submitted that the Sequence Listing and computer readable form thereof were submitted in the above-referenced application by virtue of the "Permission to Use Sequence Listing" filed January 19, 2001. However, in response to the objection that the paper copy and electronic copies of the Sequence Listing are different, Applicants are submitting a substitute copy of the computer readable form of the sequence listing of the present application and a clean paper copy of the same. The substitute paper copy is identical to the substitute copy of the computer readable form and does not include new matter to the as-filed application. Submitted concurrently is an executed statement under 37 C.F.R. §1.825(b) to that effect. Accordingly, Applicants respectfully request entry of the substitute paper copy and the substitute copy of the computer readable form of the sequence listing. In view of the above, Applicants believe that the application now complies with the requirements for sequences under 37 C.F.R. §§1.821-1.825.

B. **REJECTIONS UNDER 35 U.S.C.§112, FIRST PARAGRAPH**

Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession

of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 12 that claims 17 to 27 are directed to a vast diverse class of enzymes with structural limitations, but no specific functional limitations. (Paper No. 12, page 4).

Applicants respectfully disagree. It is alleged in the Paper No. 12 that "[t]he claims are not drawn to an aspartate transaminase having an amino acid sequence that is 70% identical to SEQ ID NO:25 for example, but to any transaminase or aminotransferase." (Paper No. 12, page 8.) Applicants respectfully submit that the claims, as pending, include both structural and functional requirements for the claimed enzyme. Structurally, the claimed enzyme must be at least 70% identical to any one of SEQ ID NOS: 25-32. Functionally, the claimed enzyme must have transaminase or aminotransferase activity. If an enzyme does not possess both of these characteristics, it falls outside of the claim. The claims are not drawn to any transaminase or aminotransferase, as alleged in Paper No. 12, but to an enzyme that is at least 70% identical to any one of SEQ ID NOS: 25-32 and has transaminase or aminotransferase activity. As such, an enzyme of the claimed invention discloses sufficient identifying characteristics to allow one of skill in the art to distinguish a transaminase or aminotransferase of the invention from a transaminase or aminotransferase that does not fall within the scope of the claims. It is respectfully submitted that claims 17, 18 and claims dependent therefrom meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, the removal of the rejection is requested.

Additionally, the Examiner's attention is drawn to new claims 28 and 29 where claims 17 and 18, respectively, are further defined. Claims 28 and 29 specify that the enzyme claimed in claim 17 and used in the method of claim 18 have the same amino group acceptor and amino group donor as the enzyme to which it is at least 70% identical. Therefore the claims provide clarification of the structural and functional limitations of the enzyme in claims 17 and 18, in order to distinguish the claimed enzymes from all other enzymes or proteins.

Similarly, Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled for a transaminase or aminotransferase having an amino acid sequence 70%, 80%, 90% or 95% identical to SEQ ID NOs: 25-32 and a method of use thereof.

Applicants respectfully draw the Examiner's attention to claims 17 and 18. As set forth above, these claims contain both structural and functional characteristics of the claimed enzyme. One of skill in the art would therefore be able to make and use the claimed invention without any undue burden. Even where there are multiple transaminase or aminotransferase activities, one of skill in the art would have known, at the time of filing of the application, how to determine whether an enzyme with at least 70% homology to any one of SEQ ID NOS: 25-32 has transaminase or aminotransferase activity or whether the enzyme does not have transaminase or aminotransferase activity. Therefore, claims 17, 18 and claims dependent therefrom meet the enablement requirement of 35 U.S.C. §112, first paragraph. Accordingly, the removal of the rejection is requested.

C. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse the rejection.

Specifically, claims 17 and 18 are rejected for recitation of "the amino acid sequence set forth in SEQ ID NOs: 25-32." In accordance with the Examiner's suggestion, claims 17 and 18 have been amended to recite "any one of SEQ ID NOs: 25-32." As such, it is respectfully requested that the rejection be removed.

Similarly, claim 18 has been rejected for recitation of "an enzyme which is at least 70% identical to the amino acid sequence." In order to clarify the claim, the claim has been amended

to recite "an enzyme encoded by an amino acid sequence which is at least 70% identical to the amino acid sequence." As such, it is respectfully requested that the rejection be removed.

Claims 23 to 27 are rejected as confusing, as claims 23 to 27 refer to an enzyme of claim 18, where claim 18 is drawn to a method. The preamble of claims 23 to 27 has been amended to recite "The method of claim 18." As such, it is respectfully submitted that claims 23 to 27 are not confusing, as amended, and it is respectfully requested that the rejection be removed.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 17 to 29 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: December 3, 2001

Lisa A. Haile, J.D., Ph.D.
Reg. No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer Number 28213

VERSION WITH MARKINGS TO SHOW CHANGES MADE

~~In~~ the specification:

On page 3:

In accordance with another aspect of the present invention there are provided isolated nucleic acid molecules encoding mature polypeptides expressed by the DNA [contained in ATCC Deposit No. _____] encoding an enzyme of the present invention.

On page 5:

[Figure 9 is a diagrammatic illustration of the assay used to assess aminotransferase activity of the proteins using glutamate dehydrogenase.] Figure 9 shows the full-length DNA (SEQ ID NO.: 35) and corresponding deduced amino acid sequence (SEQ ID NO.: 36) of *Ammonifex degensii* histidinol phosphate aminotransferase.

Figure 10 shows the full-length DNA (SEQ ID NO.: 39) and corresponding deduced amino acid sequence (SEQ ID NO.: 40) of *Aquifex* aspartate aminotransferase.

Figure 11 is a diagram of the assay used to assess aminotransferase activity of the proteins using glutamate dehydrogenase.

On page 6:

In accordance with another aspect of the present invention, there are provided isolated polynucleotides encoding the enzymes of the present invention. The deposited material is a mixture of genomic clones comprising DNA encoding an enzyme of the present invention. Each genomic clone comprising the respective DNA has been inserted into a pQE vector (Quiagen, Inc., Chatsworth, CA). [The deposit has been deposited with the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Maryland 20852, USA, on December 13, 1995 and assigned ATCC Deposit No. _____ .]

On page 22:

Transaminases are highly stereoselective, and most use L-amino acids as substrates. Using the approach disclosed in [a] commonly assigned issued U.S. Patent Number 5,939,250 [co-pending provisional application Serial No. 60/008,316, filed on December 7, 1995], filed on December 7, 1996 and entitled "Combinatorial Enzyme Development," the disclosure of which is incorporated herein by reference in its entirety, one can convert the transaminases of the invention to use D-amino acids as substrates. Such conversion makes possible a broader array of transaminase applications. For instance, D-valine can be used in the manufacture of synthetic pyrethroids. D-phenylglycine and its derivatives can be useful as components of β-lactam antibiotics. Further the thermostable transaminases have superior stability at higher temperatures and in organic solvents. Thus, they are better suited to utilize either L- and/or D-maino acids for production of optically pure chiral compounds used in pharmaceutical, agricultural, and other chemical manfactures.

On page 27:

Ammonifex degensii hp aminotransferase

5'-CCGAGAATTCATTAAAGAGGAGAAATTAACTATGGCAGTCAAAGTGCGGCCT (SEQ ID NO: 33)

3'-CGGAGGATCCTTATCCAAAGCTTCCAGGAAG (SEQ ID NO: 34)

Homology information:

Closest to *Bacillus subtilis* (reference: Henner, D.J., Band., Flaggs G., Chen E.; Gene 49:147-152(1886). Percent similarity:65.084 Percent Identity 44.134

On page 27:

Aquifex aspartate aminotransferase

5'-CCGAGAATTCATTAAAGAGGAGAAATTAACTATGAGAAAAGGACTTGCAAGT (SEQ ID NO: 37)

3'-CGGAGGATCCTTAGATCTCTTCAAGGGCTTT (SEQ ID NO: 38)

Closest to *Bacillus subtilis* (Sorkin, A.V., Azevedo, V., Zumstein, E., Galleron, N., Ehrlich, S.D. and Serror, P. Determination and analysis of the nucleotide sequence of the Bacillus subtilis chromosome region between serA and kdg loci cloned in yeast artificial chromosome Unpublished (1995). Percent similarity: 71.611 Percent identity: 52.685

In the claims:

17. (Amended) An isolated enzyme [comprising a member selected from the group consisting of an enzyme] comprising an amino acid sequence which is at least 70% identical to [the amino acid sequence set forth in] any one of SEQ ID NOS:25-32 when aligned using the BLASTN program of the National Center for Biotechnology Information, wherein the enzyme has [activity as a] transaminase or aminotransferase activity.

18. (Amended) A method for transferring an amino group from an amino acid to an α-keto acid comprising:

contacting an amino acid in the presence of an α-keto acid with an isolated enzyme selected from the group consisting of an enzyme encoded by an amino acid sequence which is at least 70% identical to [the amino acid sequence set forth in] any one of SEQ ID NOs: 25-32 when aligned using the BLASTN program of the National Center for Biotechnology Information wherein the enzyme has transaminase or aminotransferase activity; and

thereby transferring an amino group from the amino acid to the α-keto acid.

19. (Amended) An enzyme of claim 17, wherein the amino acid sequence of the isolated enzyme is at least 80% identical.

20. (Amended) An enzyme of claim 17, wherein the amino acid sequence of the isolated enzyme is at least 90% identical.

21. (Amended) An enzyme of claim 17, wherein the amino acid sequence of the isolated enzyme is at least 95% identical.

22. (Amended) An enzyme of claim 21, wherein the isolated enzyme is microbial.

23. (Amended) [An enzyme] The method of claim 18, wherein the amino acid sequence of the isolated enzyme is at least 80% identical.

24. (Amended) [An enzyme] The method of claim 18, wherein the amino acid sequence of the isolated enzyme is at least 90% identical.

25. (Amended) [An enzyme] The method of claim 18, wherein the amino acid sequence of the isolated enzyme is at least 95% identical.

26. (Amended) [An enzyme] The method of claim 25, wherein the isolated enzyme is microbial.

27. (Amended) [An enzyme] The method of claim 25, wherein the isolated enzyme converts about 400 μmoles of α-keto acid per minute per mg of the enzyme.